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**WO 02/24240 A1**

(54) Title: **SILVER CONTAINING WOUND DRESSING**

(57) Abstract: A wound dressing having anti-microbial activity comprises a first fibre capable of bonding with silver (1) cations. The wound dressing comprises a blend of the first fibre to which silver (1) cations are bonded and a second fibre which is substantially free from silver. The wound dressing comprises from 0.01 to 5.0 percent by weight of silver (1) cations, based on the weight of fibre.

## SILVER CONTAINING WOUND DRESSING

This invention relates to a wound dressing, in particular to a wound dressing having antimicrobial activity.

- International Patent Applications WO 93/12275, WO 94/16746 and PCT/GB99/02093  
5 disclose the carboxymethylation of lyocell fibre and the use of such carboxymethylated fibre in wound dressings.

European Patent Application No. 707,793 discloses a silver-containing antimicrobial agent which comprises carboxymethylcellulose containing silver in an amount of 0.02 to 1 percent by weight and having a degree of substitution of at least 0.4.

- 10 Japanese Published Unexamined Patent Application 11-001,895 discloses a hygienic product such as a disposable diaper, sanitary napkin or incontinence pad which comprises water-insoluble carboxymethylcellulose (derived from woodpulp) containing 0.32% by weight silver ions.

- 15 The silver-containing fibre used in the prior art dressings discolour (turn dark brown or black) on exposure to light. In consequence, such dressings may exhibit an unsightly appearance. Attempts have been made to overcome this problem and are described for example in International Patent Application WO 00/90173.

It is an object of the present invention to provide a wound dressing in which the above disadvantages are reduced or substantially obviated.

The present invention provides a wound dressing having anti-microbial activity, which comprises a first fibre capable of bonding with silver (1) cations, characterised in that the wound dressing comprises a blend of the first fibre to which silver (1) cations are bonded and a second fibre which is substantially free from silver.

The wound dressing according to the invention preferably comprises from 0.01 to 5%, more preferably from 0.1 to 4%, even more preferably from 0.25 to 3% by weight of silver (1) cations, based on the weight of fibre. Most preferably, the wound dressing contains 1 to 2% by weight based on fibre, of silver (1) cations, where the fibre is carboxymethyl cellulose fibre and 0.25% to 0.75% silver (1) cations, where the fibre is an alginate fibre by weight based on the weight of fibre, of silver (1) cations.

The first fibre is preferably substantially insoluble in water and preferably comprises a sodium carboxymethylcellulose fibre, an alginate fibre, a chitosan or chitosan derivative fibre or an acrylic fibre. Where the fibre is a carboxymethylcellulose fibre, it preferably has a degree of substitution between 0.1 and 0.4. Where the fibre is an acrylic fibre, it is preferably an acrylic fibre which incorporates a comonomer such as itaconic acid or 2-acrylamido methyl propane sulphonic acid to provide dye-sites in the fibre.

Where the fibre is an alginate fibre, it may be a calcium alginate fibre or a mixed metal alginate fibre such as a calcium / sodium alginate fibre. The alginate polymer may be one with a high mannuronate or a high guluronate.

Wound dressings in which the first fibre is a carboxymethylcellulose fibre are particularly preferred. The second fibre may be similar or different to the first fibre. Similar fibres are preferably used. The second fibre should be such as not to discolour to an objectionable degree in light, and as such should, for example, contain no silver or such low levels of silver that it does not discolour at all or discolours only to an degree which is not objectionable aesthetically.

The ratio of the first silver-containing fibre to the second fibre is preferably in the range from 0.5 to 25% by weight, more preferably 5 to 20% by weight, of the total weight of the fibre

In order to achieve the desired overall concentration of silver ions, the first fibre preferably includes about 10% by weight, based on the weight of fibre, of silver (I) cations and is blended with a large proportion of unsilvered fibre so as to give a blended product containing the desired weight of silver. The silver ions are preferably chemically bonded to the first  
5 fibre.

As specified above, the degree of substitution (D.S.) of the sodium carboxymethylcellulose (CMC) is preferably at least 0.1, and is preferably less than 0.4. Such CMC is inherently insoluble in water and also in saline solution. A higher D.S. gives at least partial solubility in water, which is undesirable in the field to which the invention relates. The D.S. is more  
5 preferably in the range from 0.20 to 0.35, for example about 0.3.

The silver ions are preferably introduced into the first CMC fibre by ion-exchange, for example by contacting CMC with an aqueous solution of a salt such as, silver(I) nitrate. As CMC often contains sodium chloride as a by product of the reaction between cellulose and chloroacetic acid and as silver chloride is highly insoluble. It may be preferred to perform the  
5 ion-exchange reaction on a salt free grade of CMC. It is preferred that the balance of the carboxyl groups in the CMC be neutralised with sodium ions.

The CMC is preferably derived from lyocell, as disclosed for example in WO 93/12275, WO 94/16746 and PCT/GB99/02093.

The fibrous CMC is preferably in the form of staple fibre or continuous filament yarn. It is preferably contained within a textile article such as a woven, knitted or most preferably a nonwoven fabric, such as a needlepunched nonwoven fabric.

The dressings of the invention are preferably gel-forming, which makes them advantageously low-adherent to wounds and consequently easy to remove. They are soft, conformable and absorbent. Silver metal ions are released slowly over an extended period of time from a wetted dressing of the invention.

The second fibre which does not contain silver is preferably also CMC, but other kinds of gel-forming fibre or of textile fibre may also be utilised. If the dressings are blended from unexposed fibre, on exposure to light, such dressings develop either a speckled appearance or a light brown or light grey colour which is not unsightly. However, it is preferred to pre-  
5 expose the silver-containing fibre to light before blending, so that after blending the dressing is light stable and the uniformity of blending can be checked visually.

The wound dressings of the invention may contain other medicaments if desired.

The wound dressings of the invention are useful in the treatment of infected wounds, and as a prophylactic measure against infection of uninfected wounds, also for the reduction or elimination of unpleasant odours produced by wounds.

The invention is illustrated by the following Examples, in which parts and proportions are by weight unless otherwise specified.

#### EXAMPLE 1

##### Manufacture of Master Batch Material

The optimum conditions for manufacture of a master batch material were determined as follows:

Sodium carboxy methyl cellulose fibre (CMC), Hydrocel®, available from Acordis Speciality Fibres Limited of Coventry England, was soaked in silver nitrate ( $\text{AgNO}_3$ ) solution in 50 volume % industrial methylated spirit/50 volume % water and the following table shows the percentage silver take-up after soaking, as measured by x-ray fluorescence.

% AgNO <sub>3</sub> →	4% AgNO <sub>3</sub>	8% AgNO <sub>3</sub>
Conditions ↓		
15 minutes @ 65°C	8.1	6.1
15 minutes @ ambient	12.6	11.2
4 hours @ ambient	8.0	9.0

From the above results, it was determined that higher concentrations of silver nitrate did not appear to be beneficial and that the use of a solution having a concentration of approximately 4% silver nitrate to produce a fibre having a silver content of 8% would give the optimum results. It was therefore decided to produce the master batch material using such a solution.

CMC tow or staple (50g) was added to a solution of 4% silver nitrate (300g) in industrial methylated spirit /water 50/50 at ambient temperature. The solution was held for convenience in a round screw top bottle so that it could be rolled on a laboratory bottle roller. The bottle was rolled for 15 minutes whereupon an ion exchange mechanism took place which produced silver containing CMC - referred to herein as silver CMC (8%w/w, Ag).

The spent silver nitrate solution was discarded and replaced with 50/50 industrial methylated spirit/water wash liquor (300g) followed by shaking for five minutes. This washing process was repeated and finally a soft finish was used. This consisted of 0.5% polysorbate 20 (Tween) 20 in 90:10 industrial methylated spirit/water (i.e. 1.5g in 300g).

Excess liquor was squeezed out of the fibre, which was then allowed to dry at ambient temperature. The silver CMC tow was then opened out and spread onto an open bench to allow maximum access to light. The discolouring tow was handled periodically to expose new surfaces to the light. This was continued until the majority of the tow assumed a chocolate brown coloration (about two weeks).

The predominantly brown silver CMC tow produced was blended with untreated

carboxymethyl cellulose (CMC) fibre at the ratios shown as follows to produce blends having 0.5%, 1.0% and 2.0% silver:

6.25% silver CMC + 93.75% CMC fibre = 0.5% Ag

12.5% silver CMC + 87.50% CMC fibre = 1.0% Ag

25.0% silver CMC + 75.00% CMC fibre = 2.0% Ag

Blending was accomplished by carrying out a carding operation twice to achieve a uniform blend, on hand pre-mixed fibre. The carded web was then cross-folded to give the desired basis weight. The web was then bonded on a needle loom to give a coherent web from which individual dressings were cut. In addition, a conventional carboxymethyl cellulose fibre control sample was manufactured by the same method.

#### Absorbency Results

The master batch material was produced by the soaking of CMC fibre tow in silver nitrate and the absorbency tests were first of all carried out on tow using a free swell test. It was found that the CMC fibre control had an absorbency of 28g/g and the silver CMC had an absorbency of 30g/g. These differences were not considered to be significant.

Absorbency tests were then carried out on fabric produced by needle felting from fibres as above.

Fabric absorbencies as measured by the test identified in the British Pharmacopeia 1993 Addendum 1995 page 1706, Alginate Dressing Absorbency were found to be as shown in the following table, in which gsm = grams per square metre and is a measure of the amount of fabric produced.

	gsm	Absorbency g/g	Absorbency g/piece
CMC control	111	16.0	18.0
0.5% silver CMC	99	20.0	19.5
1.0% silver CMC	91	20.5	18.7

2.0% silver CMC

65

22.3

14.5

As can be seen from the above table, the addition of silver was found to have very little effect on the absorbency, if anything increasing the absorbency on a gram per gram basis, though having less effect on absorbency on a gram per piece basis.

After wetting for 30 minutes in saline, the fabrics which were initially a fairly dark fawn, changed colour and became lighter and more translucent as time passed.

It appeared that there was no difference in the gelling properties between the CMC and the silver CMC, which is an important observation in that the silver addition does not destroy the valuable gelling properties.

#### Microbial Activity

To measure the efficiency of the silver containing material in reducing microbial activity, 250 g of milk was mixed with 0.2 g of fibre. The results were as follows:

Control (milk alone)	Malodour in 2 days
Control (CMC in milk)	Malodour in 2 days
0.5% Silver (web)	Malodour in 2 weeks
8.0% Silver (tow)	No Malodour in 3 weeks

These tests were repeated with 0.9wt% sodium chloride additions (chosen to be equivalent to the salt level in body fluids) to the milk, and the same results were obtained. This shows that the chloride ions in the salt were not detrimental to the antimicrobial properties of the silver in the silver CMC.

As can be seen from the above results, milk alone and milk containing CMC fibre alone went off in two days, as could be easily determined by the smell. By comparison, where the web contained 0.5% silver, there was a two week period before the milk went off and could be smelt. With unblended tow containing 8% silver, no smell could be detected after a three week period when the test was stopped.



In practice, the wound treatment products utilising the invention are unlikely to be left on a wound for more than a few days, and certainly no more than a week, so that it can be seen that a blend containing 0.5% silver retains its efficiency in terms of antimicrobial effect for at least twice the period that would be required in practice.

## EXAMPLE 2

A solution of water (33.1g) and industrial methylated spirit (IMS) (36.0g) was made up in a black glass bottle suitable for rolling on a bottle roller. To it was added silver nitrate (30.0g) and the latter was stirred until it dissolved. No heat was required. To this solution was added 12g of high manuronic calcium alginate tow and the whole was rolled on a bottle roller for four hours. After this period of time the tow was removed and washed in a solution (70g) containing IMS and water as a 50/50 mixture. Soft finish in the form of polysorbate 20 (0.7g) was dissolved in (70g) solution of IMS/water as a 95/5 mixture and the tow was soaked in this medium for approximately 50 minutes. The silver alginate master batch was then dried in a fume cupboard to give a product having 13.7% of silver overall on the fibre.

5g of the above silver alginate master batch was weighed and cut into staple and opened by hand. 95g of standard high manuronic calcium alginate fibre was also cut into staple and opened. The two were blended on the in-put feed belt of a laboratory carding machine.

The diluted silver alginate fibre was then carded, cross-folded and needled into a non-woven web. By calculation the final product would contain silver at an average level of 0.6%. It had a light grey-brown flecked mottled appearance.

In a comparative example, the same level (0.68%) of silver was applied uniformly to a batch of the same calcium alginate fibre, and it was then carded, cross-folded, and needled to form a nonwoven web. The web was exposed to light and developed a uniform darkish

brown colour, appearing much darker than the mottled appearance of the blended web having the same average amount of silver present.

The invention also contemplates multiple layer dressings some or all of which layers may comprise blended product incorporated silver additions. For example, a silver containing blended layer of a non-gel forming fibre, such as a silver containing acrylic fibre blended with pure acrylic fibre could be faced with a wound contact layer of a gel forming fibre. An example of the contact layer could be an alginate fibre and the alginate layer could be blended with a silver added fibre or may have no silver at all, being a simple gel forming alginate fibre.

## CLAIMS

1. A wound dressing having anti-microbial activity, which wound dressing comprises a first fibre capable of bonding with silver (1) cations, characterised in that the wound dressing comprises a blend of the first fibre to which silver (1) cations are bonded and a second fibre which is substantially free from silver.
2. A wound dressing according to claim 1 characterised in that it comprises from 0.01 to 5.0 percent by weight, of silver (1) cations based on the weight of fibre.
3. A wound dressing according to claim 2 characterised in that it comprises from 0.1 to 4.0 percent by weight of silver (1) cations based on the weight of fibre.
4. A wound dressing according to claim 3 characterised in that it comprises from 0.25 to 3.0 percent by weight of silver (1) cations based on the weight of fibre.
5. A wound dressing according to any of claims 1 to 4 characterised in that the first fibre is substantially insoluble in water.
6. A wound dressing according to any of claims 1 to 5 characterised in that the first fibre comprises a carboxymethylcellulose fibre, an alginate fibre, a chitosan or chitosan derivative fibre or an acrylic fibre.
7. A wound dressing according to claim 6 characterised in that the first fibre is a carboxymethyl cellulose fibre and the wound dressing contains from 1.0 to 2.0% by weight of silver (1) cations, based on the weight of the fibre.
8. A wound dressing according to claim 6 characterised in that the first fibre is an alginate fibre and the wound dressing contains from 0.25 to 0.75% by weight of silver (1) cations, based on the weight of the fibre.

9. A wound dressing according to claim 6 or claim 7 characterised in that the first fibre is a carboxymethylcellulose fibre which has a degree of substitution between 0.1 and 0.4.
10. A wound dressing according to claim 6 characterised in that the first fibre is an acrylic fibre which incorporates a comonomer to provide dye-sites in the fibre.
11. A wound dressing according to claim 10 characterised in that the comonomer is itaconic acid or 2-acrylamido methyl propane sulphonic acid.
12. A wound dressing according to any of claims 1 to 11 characterised in that the first fibre and the second fibre are similar.
13. A wound dressing according to any of claims 1 to 12 characterised in that the ratio of the first fibre to the second fibre is in the range of from 0.5 to 25% by weight of the total weight of the fibre.
14. A wound dressing according to claim 13 characterised in that the ratio of the first fibre to the second fibre is in the range of from 5 to 20% by weight of the total weight of the fibre.
15. A wound dressing according to any of claims 1 to 10 characterised in that the first fibre includes about 10% by weight, based on the weight of fibre, of silver (I) cations.
16. A wound dressing according to any of claims 1 to 12 characterised in that the silver ions are preferably chemically bonded to the first fibre.
17. A wound dressing according to any of claims 9 to 14 characterised in that the first fibre is a carboxymethylcellulose fibre and the degree of substitution is in the range from 0.20 to 0.35.

18. A wound dressing according to claim 14 characterised in that the degree of substitution is about 0.3.
19. A wound dressing according to any of claims 1 to 15 characterised in that the silver ions are introduced into the first fibre by ion-exchange.
20. A wound dressing according to any of claims 1 to 16 characterised in that the first fibre is a carboxymethylcellulose fibre and the carboxymethylcellulose is derived from lyocell.
21. A wound dressing according to any of claims 1 to 17 characterised in that the fibrous carboxymethylcellulose is in the form of a staple fibre or continuous filament yarn.
22. A wound dressing according to any one of the preceding claims characterised in that the carboxymethylcellulose is present in a needlepunched nonwoven textile.
23. A wound dressing substantially as herein described and with reference to the Example 5.

## INTERNATIONAL SEARCH REPORT

International Application No

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A. CLASSIFICATION OF SUBJECT MATTER  
IPC 7 A61L15/44

According to International Patent Classification (IPC) or to both national classification and IPC

## B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)

IPC 7 A61L A61F

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

WPI Data, PAJ, EPO-Internal

## C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category *	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US 6 087 549 A (FLICK A BART) 11 July 2000 (2000-07-11) column 6, line 42 -column 7, line 26 example 1 claim 1	1-23
A	WO 00 09173 A (LARSEN KIM LAMBERTSEN ;SAMUELSEN PETER BOMAN (DK); COLOPLAST AS (D) 24 February 2000 (2000-02-24) cited in the application page 1, line 4 - line 8 page 3, line 18-21 claim 1	

☐ Further documents are listed in the continuation of box C.

☒ Patent family members are listed in annex.

## \* Special categories of cited documents:

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# INTERNATIONAL SEARCH REPORT

Information on patent family members

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